

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:20:43 ON 08 APR 2005

L1 227464 S DAHLBER?/AU OR BROW?/AU OR LYAMICHEV?/AU
L2 26381 S DNA (S) CLEAVAGE
L3 930 S HAIRPIN (P) OLIGONUCLEOTIDE
L4 11 S L1 AND L3
L5 4 S L4 NOT PY>=1996
L6 2 DUP REM L5 (2 DUPLICATES REMOVED)
L7 56 S L2 AND L3
L8 19 S L7 NOT PY>=1996
L9 8 DUP REM L8 (11 DUPLICATES REMOVED)
L10 444791 S OLIGONUCLEOTIDE OR PRIMER OR PROBE OR OLIGOMER
L11 848 S L10 (S) HAIRPIN
L12 848 S L11 (P) HAIRPIN
L13 64376 S DNA (S) DETECTION
L14 56 S L2 AND L3
L15 35 S L14 AND L11
L16 35 S L14 AND L12
L17 16 S L15 NOT PY>=1996
L18 7 DUP REM L17 (9 DUPLICATES REMOVED)
L19 16 S L16 NOT PY>=1996
L20 7 DUP REM L19 (9 DUPLICATES REMOVED)
L21 22624 S HAIRPIN OR "STEM LOOP"
L22 471 S L21 AND L2
L23 9 S L22 AND L1
L24 4 DUP REM L23 (5 DUPLICATES REMOVED)
L25 1516 S "THIRD" (S) L10
L26 519 S L25 AND (CLEAVAGE OR HYBRIDIZATION OR DETECTION)
L27 265 S L26 NOT PY>=1996
L28 123 DUP REM L27 (142 DUPLICATES REMOVED)
L29 24456 S COMPLEMENTARY (S) (SEQUENCE OR REGION OR TERMIN?)
L30 9 S L28 AND L29
L31 9 DUP REM L30 (0 DUPLICATES REMOVED)

=>

L31 ANSWER 1 OF 9 MEDLINE on STN
ACCESSION NUMBER: 95373157 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7645232
TITLE: A subgenomic RNA associated with cherry leafroll virus infections.
AUTHOR: Brooks M; Bruening G
CORPORATE SOURCE: Department of Plant Pathology, College of Agricultural and Environmental Sciences, University of California, Davis 95616, USA.
SOURCE: Virology, (1995 Aug 1) 211 (1) 33-41.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U24694
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19970203
Entered Medline: 19950918

AB Cherry leafroll nepovirus (CLRV) genomic RNA 1 (8 kb) and genomic RNA 2 (7 kb) have 3' polyadenylate tracts and, extending 5' from the polyadenylate, nearly identical sequences of 1.6 kb termed the 3' common region. We observed RNAs 1 and 2 and a **third** RNA of 1.5 kb in nucleic acid extracts of CLRV-infected Nicotiana tabacum suspension cell protoplasts and Chenopodium quinoa plants, using a **hybridization probe complementary** to 1 kb of the 3' common region. The third RNA was partially purified by preparative gel electrophoresis and chromatography on an oligodeoxythymidylate column. Analyses of transcripts primed by a complementary oligodeoxyribonucleotide and of cDNA clones revealed that the third RNA corresponds to the 3' 1500 nucleotide residues of RNA 1. Hence we designate the newly characterized RNA as RNA 1A. RNA 1A was not detected as encapsidated RNA in extracts of either protoplasts or C. quinoa plants. The amount of accumulated RNA 1A declined between 24 and 48 hr after inoculation of protoplasts with CLRV virions, although CLRV RNAs 1 and 2 continued to accumulate. Other results were not consistent with cleaved RNA 1 being the origin of RNA 1A. RNA 1A has the properties of a subgenomic RNA, presumably synthesized from negative-sense RNA 1 as template.

L31 ANSWER 2 OF 9 MEDLINE on STN
ACCESSION NUMBER: 95174196 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7869595
TITLE: **Detection** of Campylobacter species by using polymerase chain reaction and nonradioactive DNA probes. III. DNA probe for identification of C. laridis.
AUTHOR: Yamashita K; Takarada Y; Otsuka N; Kagawa S; Matsuoka A
CORPORATE SOURCE: Clinical Laboratory, Hyogo College of Medicine, Nishinomiya.
SOURCE: Rinsho byori. Japanese journal of clinical pathology, (1994 Dec) 42 (12) 1294-8.
Journal code: 2984781R. ISSN: 0047-1860.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950407
Last Updated on STN: 19950407
Entered Medline: 19950328

AB The development of a rapid and specific DNA probe assay for identification of Campylobacter species, including C. jejuni, C. coli, C. laridis, C. fetus, and C. hyointestinalis is important in determining the precise diagnosis of Campylobacter infections. **Sequence** data of our previous studies for a 240-base DNA fragment was used to select primers and probes conjugated to alkaline phosphatase, **complementary** to a portion of DNA between primers. However, a 21-base probe (CL (1))

tested here for **detection** of *C. laridis* was cross-reactive with PCR-amplified fragments of *C. jejuni*, *C. coli* and *C. hyointestinalis*, although it was not reactive with *C. fetus* and *C. fetus* subsp. *fetus*. To solve this problem, further modifications of the probe were therefore made to improve the specificity for those particular species. A second 21-base **probe** with a single base-substitution (CL (2)) and a **third** 20-base **probe** (CL(3)) were ineffective for identification of *C. laridis*, too. A fourth 20-base probe with a single base substitution (CL(4)) was a significant improvement over the results obtained by other three probes specifically to detect *C. laridis*. Thus, the alkaline phosphatase-labeled probe method developed so far is an interesting alternative without access to radioisotopes for clinical laboratories for identification of *Campylobacter* species, including *C. jejuni/coli/hyointestinalis*, *C. laridis*, and *C. fetus/fetus* subsp. *fetus*.

L31 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:78160 BIOSIS
DOCUMENT NUMBER: PREV199497091160
TITLE: Isolates of viral hemorrhagic septicemia virus from North America and Europe can be detected and distinguished by DNA probes.
AUTHOR(S): Batts, W. N. [Reprint author]; Arakawa, C. K. [Reprint author]; Bernard, J.; Winton, J. R. [Reprint author]
CORPORATE SOURCE: Natl. Fish. Res. Cent., Build. 204 Naval Station, Seattle, WA 98115, USA
SOURCE: Diseases of Aquatic Organisms, (1993) Vol. 17, No. 1, pp. 67-71.
CODEN: DAOREO. ISSN: 0177-5103.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1994
Last Updated on STN: 22 Feb 1994

AB Biotinylated DNA probes were constructed to hybridize with specific sequences within the messenger RNA (mRNA) of the nucleoprotein (N) gene of viral hemorrhagic septicemia virus (VHSV) reference strains from Europe (07-71) and North America (Makah). Probes were synthesized that were **complementary** to: (1) a 29-nucleotide **sequence** near the center of the N gene common to both the 07-71 and Makah reference strains of the virus; (2) a unique 28-nucleotide **sequence** that followed the open reading frame of the Makah N gene mRNA, most of which was absent in the 07-71 strain; and (3) a 22-nucleotide **sequence** within the 07-71 N gene that had 6 mismatches with the Makah strain. Sixteen diverse isolates of VHSV from North America and Europe were tested by dot blot **hybridization**. The first **probe** reacted with all isolates of the virus, the second **probe** reacted with only the North American isolates (including those from Pacific cod), and the **third probe** reacted with only the European isolates, including those from rainbow trout, brown trout and Atlantic cod. The probes did not react with mRNA extracted from uninfected cells or from cells infected with infectious hematopoietic necrosis virus (IHNV), a related fish rhabdovirus. The results showed that VHSV isolates from North America and Europe formed 2 genetically distinct strains of the virus in which isolates from different years or species of fish on each continent were more related to each other than to isolates from the other continent. The results of this and other studies indicate that the North American strain of VHSV is enzootic in the North Pacific Ocean and is not a result of a recent importation of fish from Europe. When used in conjunction with a biotinylated probe that recognizes all isolates of IHNV, these reagents promise to simplify the **detection** of salmonid rhabdoviruses.

L31 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 93004736 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1391945
TITLE: **Detection** and quantitation of malignant cells in the peripheral blood of multiple myeloma patients.
AUTHOR: Billadeau D; Quam L; Thomas W; Kay N; Greipp P; Kyle R; Oken M M; Van Ness B

CORPORATE SOURCE: Department of Biochemistry, School of Public Health,
University of Minnesota, Minneapolis 55455.

CONTRACT NUMBER: CA 21115 (NCI)
GM 37687 (NIGMS)

SOURCE: Blood, (1992 Oct 1) 80 (7) 1818-24.
Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199210

ENTRY DATE: Entered STN: 19930122

Last Updated on STN: 19930122

Entered Medline: 19921029

AB One of the distinguishing features of multiple myeloma (MM) is the proliferation of plasma cells that home to the bone marrow (BM). However, there still remains some uncertainty concerning the presence of related malignant cells in the peripheral blood of myeloma patients. Using consensus **oligonucleotide** primers, we amplified the **third complementary** determining region (CDR3) of rearranged immunoglobulin heavy chain alleles from MM marrow samples by polymerase chain reaction (PCR). From the sequences of the products, we derived allele-specific oligonucleotides (ASO), and these were used in subsequent amplification reactions to detect malignant clones in the peripheral blood of myeloma patients. This method is highly specific and sensitive to 1 malignant cell in the background of 10(5) normal cells. Using this method we detected circulating malignant cells in 13 of 14 previously untreated MM patients. Furthermore, by applying ASO-PCR to artificial titrations of initial BM DNA sample into normal peripheral blood lymphocyte (PBL) DNA we were able to generate standard curves and quantitate the amount of tumor in the patient PBL. We observed a wide variation in the amount of circulating tumor between patients. In addition, we found that the incidence of circulating tumor cells was independent of BM tumor burden and stage of disease. The **detection** and quantitation of circulating tumor cells in the PBL of MM patients may offer an alternative assessment of the disease and may be an important consideration in the use of peripheral stem cells in bone marrow transplantation.

L31 ANSWER 5 OF 9

MEDLINE on STN

ACCESSION NUMBER: 91365862 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1890169

TITLE: **Detection** of Helicobacter pylori by using the
polymerase chain reaction.

AUTHOR: Valentine J L; Arthur R R; Mobley H L; Dick J D

CORPORATE SOURCE: Department of Immunology and Infectious Diseases. Johns
Hopkins School of Public Health and Hygiene, Baltimore,
Maryland.

SOURCE: Journal of clinical microbiology, (1991 Apr) 29 (4) 689-95.
Journal code: 7505564. ISSN: 0095-1137.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199110

ENTRY DATE: Entered STN: 19911103

Last Updated on STN: 19911103

Entered Medline: 19911015

AB A 1.9-kb cloned fragment of chromosomal DNA randomly selected from a Helicobacter pylori cloned library was evaluated as a potential probe. The probe detected 19 of 19 H. pylori strains and yielded a specificity of 98.7% when tested against 306 other bacterial strains representing 32 different species. False-positive results with non-H. pylori strains were due to the presence of contaminating vector sequences. A polymerase chain reaction (PCR) assay was developed by using 20-base oligonucleotide primers homologous to a portion of the 1.9-kb fragment. The PCR assay amplified a 203-nucleotide-pair product which was analyzed by agarose gel electrophoresis and Southern **hybridization** by using a

third 20-base 32P-labeled oligonucleotide

complementary to a **region** of DNA between the primers.

The PCR assay was 100% sensitive, detecting all 35 *H. pylori* strains tested, and did not amplify sequences in several closely related species. The assay was sensitive for as little as one copy of the cloned plasmid DNA or 100 *H. pylori* bacterial cells. To evaluate the PCR assay for clinical samples, gastric biopsy and aspirate specimens were tested by PCR, and the results were compared with those of microbiologic culture and histologic examination. In fresh biopsy specimens, *H. pylori* sequences were detected by PCR in 13 of 14 (93%) positive tissues and 0 of 19 negative tissues. In gastric aspirate specimens, 11 of 13 (85%) positive tissues were positive by PCR. *H. pylori* DNA was detected in 1 of 14 aspirate specimens negative by culture, histology, and PCR of the accompanying biopsy tissue. PCR is a rapid, accurate, and sensitive method for the **detection** of *H. pylori*.

L31 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 91306442 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1713000
TITLE: Mutations in a satellite RNA of turnip crinkle virus result in addition of poly(U) in vivo.
AUTHOR: Carpenter C D; Cascone P J; Simon A E
CORPORATE SOURCE: Department of Biochemistry, University of Massachusetts, Amherst 01003.
SOURCE: Virology, (1991 Aug) 183 (2) 595-601.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910908
Last Updated on STN: 19970203
Entered Medline: 19910819

AB Turnip crinkle virus (TCV) is associated with many subviral RNAs including satellite (sat-) RNAs which require a helper virus for infectivity. When plants were inoculated with TCV and transcripts of TCV sat-RNA C containing deletions of 3 to 8 nucleotides beginning at position 100 and extending toward the 5' end, some of the sat-RNA isolated from plants migrated more slowly than expected on denaturing polyacrylamide gels. **Cleavage** of the sat-RNA into two segments by digestion with RNase H following **hybridization** to an **oligonucleotide complementary** to internal sat-RNA **sequence** indicated that the 5' one-third of the molecule was involved in the abnormal gel migration. Sat-RNAs derived from transcripts with a deletion of bases in position 96-100 were cloned. Sequencing of the cDNAs revealed that the aberrant migration of the sat-RNAs was due to the presence of variable lengths of poly(U) 10 nucleotides downstream from the deletion at a position which already contained five U residues. Deletions extending toward the 3' end in the same region did not result in poly(U) additions. Mutations in the original five U residues along with the 5' deletions also did not lead to poly(U) additions. The insertion of poly(U) in TCV sat-RNA C may be a new example of replicase stuttering with the distinction that it only occurs following specific upstream mutations.

L31 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 88124968 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3277186
TITLE: Human promyelocytic leukemia HL-60 cell proliferation and c-myc protein expression are inhibited by an antisense pentadecadeoxynucleotide targeted against c-myc mRNA.
AUTHOR: Wickstrom E L; Bacon T A; Gonzalez A; Freeman D L; Lyman G H; Wickstrom E
CORPORATE SOURCE: Department of Chemistry, University of South Florida, Tampa 33620.
CONTRACT NUMBER: CA42960 (NCI)
RR07121 (NCRR)
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1988 Feb) 85 (4) 1028-32.
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880321

AB The human promyelocytic leukemia cell line HL-60 overexpresses the c-myc protooncogene. A calculated secondary structure for c-myc mRNA placed the initiation codon in a bulge of a weakly base-paired region. Treatment of HL-60 cells with 5' d(AACGTTGAGGGGCAT) 3', complementary to the initiation codon and the next four codons of c-myc mRNA, inhibited c-myc protein expression in a dose-dependent manner. However, treatment of HL-60 cells with 5' d(TTGGGATAACACTTA) 3', complementary to nucleotides 17-31 of vesicular stomatitis virus matrix protein mRNA, displayed no such effects. These results agree with analogous studies of normal human T lymphocytes [Heikkila, R., Schwab, G., Wickstrom, E., Loke, S. L., Pluznik, D. H., Watt, R. & Neckers, L. M. (1987) Nature (London) 328, 445-449], except that only one-third as much **oligomer** was needed for a comparable effect. Proliferation of HL-60 cells in culture was inhibited in a **sequence**-specific, dose-dependent manner by the c-myc-**complementary** oligomer, but neither the oligomer **complementary** to vesicular stomatitis virus matrix protein mRNA nor 5' d(CATTCTTGCTCTCC) 3', **complementary** to nucleotides 5399-5413 of human immunodeficiency virus tat gene mRNA, inhibited proliferation. It thus appears that antisense oligodeoxynucleotides added to myc-transformed cells via culture medium are capable of eliciting sequence-specific, dose-dependent inhibition of c-myc protein expression and cell proliferation.

L31 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 81186286 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6261960
TITLE: A unique cap(m7GpppXm)-dependent influenza virion endonuclease cleaves capped RNAs to generate the primers that initiate viral RNA transcription.
AUTHOR: Plotch S J; Bouloy M; Ulmanen I; Krug R M
SOURCE: Cell, (1981 Mar) 23 (3) 847-58.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198107
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810720

AB We propose a mechanism for the priming of influenza viral RNA transcription by capped RNAs in which specific 5'-terminal fragments are cleaved from the capped RNAs by a virion-associated endonuclease. These fragments would serve as the actual primers for the initiation of transcription by the initial incorporation by the initial incorporation of a G residue at their 3' end. We show that virions and purified viral cores contain a unique endonuclease that cleaves RNAs containing a 5' methylated cap structure (m7GpppXm) preferentially at purine residues 10 to 14 nucleotides from the cap, generating fragments with 3'-terminal hydroxyl groups. RNAs containing the 5'-terminal structure GpppG could not be cleaved to produce these specific fragments. Consistent with our proposed mechanism, those capped fragments that function as primers could be linked to a G residue in transcriptase reactions containing alpha-32P-GTP as the only ribonucleoside triphosphate. The pattern of G and C incorporation onto these **primer** fragments suggests that this incorporation is directed by the second and **third** bases at the 3' end of the virion RNA template, which has the sequence 3' UCG. Primer fragments with a 3'-**terminal** A residue were used more

efficiently than those with a 3'-**terminal** G residue, indicating a preference for generating an AGC **sequence** in the viral mRNA **complementary** to the 3' end of the virion RNA. **Cleavage** of the RNA primer and initiation of transcription are not necessarily coupled, because a 5' fragment isolated from one reaction could be used as a primer when added to a second reaction. Uncapped ribopolymer inhibitors of viral RNA transcription inhibited the **cleavage** of capped RNAs.

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ACCESSION NUMBER: 80032447 EMBASE
DOCUMENT NUMBER: 1980032447
TITLE: Evidence for the identity of shared 5'-terminal sequences between genome RNA and subgenomic mRNA's of B77 avian sarcoma virus.
AUTHOR: Stoltzfus C.M.F.; Kuhnert L.K.
CORPORATE SOURCE: Dept. Microbiol., Vanderbilt Univ. Sch. Med., Nashville, Tenn. 37232, United States
SOURCE: Journal of Virology, (1979) Vol. 32, No. 2, pp. 536-545.
CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 047 Virology
016 Cancer
022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB The polyribosomal fraction from chicken embryo fibroblasts infected with B77 avian sarcoma virus contained 38S, 28S, and 21S virus-specific RNAs in which sequences identical to the 5'-terminal 101 bases of the 38S genome RNA were present. The only polyadenylic acid-containing RNA species with 5' sequences which was detectable in purified virions had a sedimentation coefficient of 38S. This evidence is consistent with the hypothesis that a leader sequence derived from the 5' terminus of the RNA is spliced to the bodies of the 28S and 21S mRNA's, both of which have been shown previously to be derived from the 3' terminal half of the 38S RNA. The entire 101-base 5'terminal sequence of the genome RNA appeared to be present in the majority of the subgenomic intracellular virus-specific mRNA's, as established by several different methods. First, the extent of **hybridization** of DNA **complementary** to the 5'-**terminal** 101 bases of the genome to polyadenylic acid-containing subgenomic RNA was similar to the extent of its **hybridization** to 38S RNA from infected cells and from purified virions. Second, the fraction of the total cellular polyadenylic acid-containing RNA with 5' sequences was similar to the fraction of RNA containing sequences identical to the extreme 3' **terminus** of the genome RNA when calculated by the rate of **hybridization** of the appropriate **complementary** DNA probes. This suggests that most intracellular virus-specific RNA molecules contain sequences identical to those present in the 5'-terminal 101 bases of the genome. **Third**, the size of most of the radioactively labeled DNA **complementary** to the 5'-**terminal** 101 bases of the genome remained unchanged after the **probe** was annealed to either intracellular 38S RNA or to various size classes of subgenomic RNA and the hybrids were digested with S1 nuclease and denatured with alkali. However, after this procedure some DNA fragments of lower molecular weight were present. This was not the case when the DNA **complementary** to the 5'-**terminal** 101 bases of the genome was annealed to 38S genome RNA. These results suggest that, although the majority of intracellular RNA contains the entire 101-base 5'-terminal leader sequence, a small population of virus-specific RNAs exist that contain either a shortened 5'leader sequence or additional splicing in the terminal 101 bases.

L20 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 96032641 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7547989
TITLE: Double-stranded damage of DNA.RNA hybrids by
neocarzinostatin chromophore: selective C-1' chemistry on
the RNA strand.
AUTHOR: Zeng X; Xi Z; Kappen L S; Tan W; Goldberg I H
CORPORATE SOURCE: Department of Biological Chemistry and Molecular
Pharmacology, Harvard Medical School, Boston, Massachusetts
02115, USA.
CONTRACT NUMBER: CA44257 (NCI)
SOURCE: Biochemistry, (1995 Sep 26) 34 (38) 12435-44.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951106

AB Glutathione-activated neocarzinostatin chromophore generates bistranded lesions in the hybrid formed by yeast tRNA(phe) and DNA complementary to its 31-mer 3' terminus. To elucidate the chemistry of the RNA cleavage reaction and to show that the lesions are double-stranded (ds), a series of shorter oligoribonucleotides containing the target sequence r(AGAAUUC).(GAATTCT) (underlining indicates major attack site) was studied as substrates. In addition to cleavage at both U residues, major damage was produced in the form of an abasic site at the U residues. Evidence for abasic site formation on the RNA strand was obtained from sequencing-gel analysis and measurement of uracil base release. Initial evidence for the ds nature of the damage came from experiments in which 2'-O-methyluridine was substituted for uridine in the RNA at one or both of the target sites. The site containing the substitution was not a target for **cleavage** or abasic site formation, and the particular T residue, staggered two nucleotides in the 3' direction on the complementary **DNA** strand, was cleaved significantly less. These studies were valuable in identifying the DNA ds partner of the RNA attack site. Direct evidence for ds lesions came from analysis of the products from a **hairpin oligonucleotide** construct in which the RNA and DNA strands were linked by four T residues and contained an internal 32P label at the 3' end of the RNA strand. Substitution of deuterium for hydrogen at the C-1' position of the U residues led to a substantial isotope effect ($k_{1H}/k_{2H} = 3$) upon the formation of the RNA abasic lesion and the RNA cleavage products, providing conclusive evidence for selective 1' chemistry. On the other hand, **cleavage** at the T residues on the complementary **DNA** strand involved C-5' hydrogen abstraction, as was also true for the T residue in an oligodeoxynucleotide analogue of the RNA strand. Chemical mechanisms to account for the RNA cleavage and abasic site formation via C-1' hydrogen abstraction are proposed.

L20 ANSWER 2 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 95247603 EMBASE
DOCUMENT NUMBER: 1995247603
TITLE: The trinucleotide repeat sequence d(GTC)15 adopts a hairpin conformation.
AUTHOR: Yu A.; Dill J.; Wirth S.S.; Huang G.; Lee V.H.; Haworth I.S.; Mitas M.
CORPORATE SOURCE: Dept. Biochemistry Molecular Biology, Oklahoma State University, 246 Noble Research Center, Stillwater, OK 74078, United States
SOURCE: Nucleic Acids Research, (1995) Vol. 23, No. 14, pp. 2706-2714.
ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950906
Last Updated on STN: 950906

AB The structure of a single-stranded (ss) **oligonucleotide** containing (GTC)15 [SS(GTC)15] was examined. As a control, parallel studies were performed with ss(CTG)15, an **oligonucleotide** that forms a **hairpin**. Electrophoretic mobility, KMnO4 oxidation and P1 nuclease studies demonstrate that, similar to ss(CTG)15, ss(GTC)15 forms a **hairpin** containing base paired and/or stacked thymines in the stem. Electrophoretic mobility melting profiles performed in .apprx. 1 mM Na+ revealed that the melting temperatures of ss(GTC)15 and ss(CTG)15 were 38 and 48°C respectively. The loop regions of ss(GTC)15 and ss(CTG)15 were cleaved by single-strand-specific P1 nuclease at the T25-C29 and G26-C27 phosphodiester bonds respectively (where the loop apex of the DNAs is T28). Molecular dynamics simulations suggested that in ss(GTC)15 the loop was bent towards the major groove of the stem, apparently causing an increased exposure of the T25-C29 region to solvent. In SS(CTG)15 guanine-guanine stacking caused a separation of the G26 and C27 bases, resulting in exposure of the intervening phosphodiester to solvent. The results suggest that ss(GTC)15 and SS(CTG)15 form similar, but distinguishable, **hairpin** structures.

L20 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 95119015 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7819224
TITLE: Recognition and **cleavage** of single-stranded DNA containing hairpin structures by oligonucleotides forming both Watson-Crick and Hoogsteen hydrogen bonds.
AUTHOR: Francois J C; Helene C
CORPORATE SOURCE: Laboratoire de Biophysique, Museum National d'Histoire Naturelle, INSERM U 201, CNRS UA 481, Paris, France.
SOURCE: Biochemistry, (1995 Jan 10) 34 (1) 65-72.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950216

AB A new approach is described to design antisense oligonucleotides targeted against single-stranded nucleic acids containing **hairpin** structures by use of both Watson-Crick and Hoogsteen hydrogen bond interactions for recognition. The **oligonucleotide** has two different domains, one allowing double helix formation involving Watson-Crick base pairs and the other one forming a triple helix involving Hoogsteen-type base triplets in the major groove of a **hairpin** stem. Spectroscopic and gel retardation experiments provided evidence for such Watson-Crick/Hoogsteen (WC/H) recognition of **hairpin** structures in single-stranded DNA. An antisense **oligonucleotide** designed to form only Watson-Crick base pairs was unable to disrupt the stable stem structure of the target under conditions where the **oligonucleotide** designed with the Watson-Crick/Hoogsteen interactions could bind efficiently to the **hairpin**-containing target. The addition of one nucleotide to the **oligonucleotide** at the junction between the double helix and triple helix regions in WC/H complexes had an effect on stability which was dependent on the relative orientation of the Watson-Crick and Hoogsteen domains in the target. An oligodeoxynucleotide-phenanthroline conjugate targeted against such a **hairpin**-containing DNA fragment induced specific **cleavage** in the double-stranded stem. This WC/H approach may be useful in designing artificial regulators of gene expression.

L20 ANSWER 4 OF 7 MEDLINE on STN - DUPLICATE 3
 ACCESSION NUMBER: 94171808 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8125998
 TITLE: Site-specific **cleavage** of a **DNA** hairpin
 by topoisomerase II. **DNA** secondary structure as a
 determinant of enzyme recognition/**cleavage**.
 AUTHOR: Froelich-Ammon S J; Gale K C; Osheroff N
 CORPORATE SOURCE: Department of Biochemistry, Vanderbilt University School of
 Medicine, Nashville, Tennessee 37232-0146.
 CONTRACT NUMBER: 5 T32 CA09582 (NCI)
 GM33944 (NIGMS)
 SOURCE: Journal of biological chemistry, (1994 Mar 11) 269 (10)
 7719-25.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199404
 ENTRY DATE: Entered STN: 19940420
 Last Updated on STN: 19940420
 Entered Medline: 19940412

AB To further define the nucleic acid determinants that govern the
 recognition of DNA by topoisomerase II, the ability of the enzyme to
 cleave a 51-base **oligonucleotide** that contained a centrally
 located 19-base **hairpin** was characterized. Topoisomerase II
 cleaved the 51-mer in a site-specific fashion, within the **hairpin**
 , one nucleotide from the 3'-base of the stem. Protein denaturants were
 not required to trap cleavage products. Although the sequence of the
oligonucleotide influenced levels of enzyme-mediated **DNA**
 scission, it did not affect the spatial location of **cleavage**.
 DNA scission required a double-stranded/single-stranded junction at the
 3'-base of the **hairpin** and a tail (either single- or
 double-stranded) at least 8 bases in length on the 5'-side. Cleavage was
 not observed when base-pairing within the **oligonucleotide** was
 eliminated or when the **hairpin** was extended to produce a
 completely double-stranded substrate. Finally, the enzyme displayed a
 size constraint for both the stem and loop structures of the
hairpin. These results indicate that topoisomerase II is capable
 of recognizing secondary structure within nucleic acids and identifies the
 first secondary structure-specific **DNA** recognition/
cleavage site for the type II enzyme.

L20 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 95023154 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7937117
 TITLE: Recognition and cleavage of hairpin structures in nucleic
 acids by oligodeoxynucleotides.
 AUTHOR: Francois J C; Thuong N T; Helene C
 CORPORATE SOURCE: Laboratoire de Biophysique, INSERM U.201, CNRS U.A. 481,
 Paris.
 SOURCE: Nucleic acids research, (1994 Sep 25) 22 (19) 3943-50.
 Journal code: 0411011. ISSN: 0305-1048.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199411
 ENTRY DATE: Entered STN: 19941222
 Last Updated on STN: 19941222
 Entered Medline: 19941116

AB The possibility of designing antisense oligodeoxynucleotides complementary
 to non-adjacent single-stranded sequences containing **hairpin**
 structures was studied using a DNA model system. The structure and
 stability of complexes formed by a 17mer **oligonucleotide** with
DNA fragments containing **hairpin** structures was
 investigated by spectroscopic measurements (melting curves) and chemical

reactions (osmium tetroxide reaction, copper-phenanthroline cleavage). A three-way junction was formed when the **oligonucleotide** was bound to both sides of the **hairpin** structure. When the complementary sequences of the two parts of the **oligonucleotide** were separated by a sequence which could not form a **hairpin**, the **oligonucleotide** exhibited a slightly weaker binding than to the **hairpin**-containing target. An oligodeoxynucleotide-phenanthroline conjugate was designed to form Watson-Crick base pairs with two single-stranded regions flanking a **hairpin** structure in a DNA fragment. In the presence of Cu²⁺ ions and a reducing agent, two main cleavage sites were observed at the end of the duplex structure formed by the **oligonucleotide**-phenanthroline conjugate with its target sequence. Competition experiments showed that both parts of the **oligonucleotide** must be bound in order to observe sequence-specific cleavage. Cleavage was still observed with target sequences which could not form a **hairpin**, provided the reaction was carried out at lower temperatures. These results show that sequence-specific recognition and modification (cleavage) can be achieved with antisense oligonucleotides which bind to non-adjacent sequences in a single-stranded nucleic acid.

L20 ANSWER 6 OF 7 MEDLINE on STN
 ACCESSION NUMBER: 93144894 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 1283351
 TITLE: Sequence-specific **cleavage** of single-stranded **DNA** by oligonucleotides conjugated to bleomycin.
 AUTHOR: Sergeev D S; Zarytova V F; Mamaev S V; Godovikova T S; Vlassov V V
 CORPORATE SOURCE: Institute of Bioorganic Chemistry, Siberian Division of the Russian Academy of Sciences, Novosibirsk.
 SOURCE: Antisense research and development, (1992 Fall) 2 (3) 235-41.
 Journal code: 9110698. ISSN: 1050-5261.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199303
 ENTRY DATE: Entered STN: 19930312
 Last Updated on STN: 19960129
 Entered Medline: 19930302

AB **Cleavage** of a single-stranded **DNA** fragment by complementary oligonucleotides conjugated to bleomycin A5 has been investigated. The conjugates efficiently cleave the DNA at the GT sequences near the **oligonucleotide** binding site. The temperature dependence of the reaction and the composition of the degradation products indicate that the **oligonucleotide**-linked bleomycin attacks the available double-stranded DNA regions within the **oligonucleotide**-DNA duplex and in the **hairpin** DNA region in the vicinity of the carrier **oligonucleotide** binding site.

L20 ANSWER 7 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN DUPLICATE 5
 ACCESSION NUMBER: 82168608 EMBASE
 DOCUMENT NUMBER: 1982168608
 TITLE: Strategies for constructing complementary DNA for cloning.
 AUTHOR: Gaubatz J.; Paddock G.V.
 CORPORATE SOURCE: Dept. Biochem., Coll. Med., Univ. South Alabama, Mobile, AL 36688, United States
 SOURCE: Journal of Theoretical Biology, (1982) Vol. 95, No. 4, pp. 679-696.
 CODEN: JTBIAP
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 022 Human Genetics
 LANGUAGE: English
 ENTRY DATE: Entered STN: 911209
 Last Updated on STN: 911209

AB We have examined alternative approaches to existing methods for synthesizing complementary DNA suitable for molecular cloning. One model of construction is presented in which ribonucleotides are added to the 3' end of complementary DNA prior to synthesis of the second DNA strand. The **hairpin** structure at one end of the molecule is then opened by treatment with RNase or alkali. This method would eliminate the normal requirement for single-strand specific nucleases and thus shows promise as a means for preserving the 5' end sequences of mRNA in recombinant complementary DNA studies. Another technique for constructing complementary DNA is proposed in which no **cleavage** step is required. Instead, a **hairpin**, double-stranded DNA is extended with a homopolymer at the 3' end, and displacement or 'third-strand' synthesis by the Klenow fragment of DNA polymerase I is primed by an **oligonucleotide** hybridized to the homopolymer. The end result should be an inverted repeat with two-fold rotational symmetry. The mRNA 5' end sequences represent the center of symmetry. Cloned, symmetrical DNA should facilitate subsequent nucleotide sequence analysis. Furthermore, the symmetrical molecule may serve as an intermediate in continued DNA synthesis provided the homopolymer chain is sufficiently longer than the primer, thus leading to mRNA sequence amplification in vitro. Alternative options with attendant advantages and disadvantages are given at each stage in the construction schemes. These strategies, along with established procedures, offer a repertoire from which researchers may select in order to fill their specific needs.

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L24 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003188389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12706715
TITLE: Modeling of flap endonuclease interactions with DNA
substrate.
AUTHOR: Allawi Hatim T; Kaiser Michael W; Onufriev Alexey V; Ma
Wu-Po; Brogaard Andrew E; Case David A; Neri Bruce P;
Lyamichev Victor I
CORPORATE SOURCE: Third Wave Technologies, Inc., 502 S Rosa Road, Madison, WI
53719, USA.. hallawi@twi.com
SOURCE: Journal of molecular biology, (2003 May 2) 328 (3) 537-54.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030423
Last Updated on STN: 20030513
Entered Medline: 20030509

AB Structure-specific 5' nucleases play an important role in DNA replication and repair uniquely recognizing an overlap flap DNA substrate and processing it into a DNA nick. However, in the absence of a high-resolution structure of the enzyme/DNA complex, the mechanism underlying this recognition and substrate specificity, which is key to the enzyme's function, remains unclear. Here, we propose a three-dimensional model of the structure-specific 5' flap endonuclease from *Pyrococcus furiosus* in its complex with DNA. The model is based on the known X-ray structure of the enzyme and a variety of biochemical and molecular dynamics (MD) data utilized in the form of distance restraints between the enzyme and the DNA. Contacts between the 5' flap endonuclease and the sugar-phosphate backbone of the overlap flap substrate were identified using enzyme activity assays on substrates with methylphosphonate or 2'-O-methyl substitutions. The enzyme footprint extends two to four base-pairs upstream and eight to nine base-pairs downstream of the **cleavage** site, thus covering 10-13 base-pairs of duplex DNA. The footprint data are consistent with a model in which the substrate is bound in the DNA-binding groove such that the downstream duplex interacts with the helix-**hairpin**-helix motif of the enzyme. MD simulations to identify the substrate orientation in this model are consistent with the results of the enzyme activity assays on the methylphosphonate and 2'-O-methyl-modified substrates. To further refine the model, 5' flap endonuclease variants with alanine point substitutions at amino acid residues expected to contact phosphates in the substrate and one deletion mutant were tested in enzyme activity assays on the methylphosphonate-modified substrates. Changes in the enzyme footprint observed for two point mutants, R64A and R94A, and for the deletion mutant in the enzyme's beta(A)/beta(B) region, were interpreted as being the result of specific interactions in the enzyme/DNA complex and were used as distance restraints in MD simulations. The final structure suggests that the substrate's 5' flap interacts with the enzyme's helical arch and that the helix-**hairpin**-helix motif interacts with the template strand in the downstream duplex eight base-pairs from the cleavage site. This model suggests specific interactions between the 3' end of the upstream oligonucleotide and the enzyme. The proposed structure presents the first detailed description of substrate recognition by structure-specific 5' nucleases.

L24 ANSWER 2 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2001151508 EMBASE
TITLE: The scid recombination-inducible cell line: A model to
study DNA-PK-independent V(D)J recombination.
AUTHOR: **Brown M.L.**; Lew S.; Chang Y.
CORPORATE SOURCE: Y. Chang, Arizona State University, Department of
Microbiology, Prog. in Molecular/Cellular Biology, Tempe,
AZ 85287-2701, United States. yung.chang@asu.edu

SOURCE: Immunology Letters, (1 Dec 2000) Vol. 75, No. 1, pp. 21-26.
Refs: 48
ISSN: 0165-2478 CODEN: IMLED6
PUBLISHER IDENT.: S 0165-2478(00)00283-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010510
Last Updated on STN: 20010510

AB To investigate the molecular mechanisms of the variable (diversity) joining (V(D)J) recombination process at an endogenous gene locus, recombination-inducible cell lines were made from both bcl-2-bearing severe combined immune deficiency (scid) homozygous and scid heterozygous (s/+) mice by transforming pre-B cells with the temperature-sensitive Abelson murine leukemia virus (ts-Ab-MLV). These transformants can be induced to undergo immunoglobulin light-chain gene rearrangements by incubating them at the non-permissive temperature. In the case of transformed scid cells, a significant amount of **hairpin** coding ends are accumulated during recombination induction, but few coding joints are generated. After being shifted to the permissive temperature, however, these cells are capable of opening **hairpin** ends and forming coding joints. Thus, ts-Ab-MLV transformed scid cells can be readily manipulated for both recombination cleavage and end resolution. However, unlike the rapid coding joint formation in s/+ cells that have the catalytic subunit of DNA-dependent protein kinase (DNA-PKcs), the process for resolving coding ends in scid cells is slow and error prone, and also appears to be correlated with a reduction in the RAG1/2 expression. Apparently, this process is mediated by a DNA-PK-independent pathway. The fact that the activity of this pathway can be manipulated in vitro makes it possible to delineate the mechanisms in end opening, processing and joining. Therefore, these ts-Ab-MLV transformed scid cell lines offer a model to study the molecular nature as well as the regulation of the DNA-PK-independent pathway in coding end resolution.
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L24 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998449971 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9774698
TITLE: Failure of **hairpin**-ended and nicked DNA To
activate DNA-dependent protein kinase: implications for
V(D)J recombination.
AUTHOR: Smider V; Rathmell W K; **Brown G**; Lewis S; Chu G
CORPORATE SOURCE: Departments of Medicine and Biochemistry, Stanford
University Medical Center, Stanford, California 94305, USA.
SOURCE: Molecular and cellular biology, (1998 Nov) 18 (11) 6853-8.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20020420
Entered Medline: 19981123

AB V(D)J recombination is initiated by a coordinated **cleavage** reaction that nicks **DNA** at two sites and then forms a **hairpin** coding end and blunt signal end at each site. Following **cleavage**, the **DNA** ends are joined by a process that is incompletely understood but nevertheless depends on **DNA**-dependent protein kinase (**DNA-PK**), which consists of Ku and a 460-kDa catalytic subunit (**DNA-PKCS** or p460). Ku directs **DNA-PKCS** to **DNA** ends to efficiently activate the kinase. In vivo, the mouse SCID mutation in **DNA-PKCS** disrupts joining of the **hairpin** coding ends but spares joining of the open signal ends. To better

understand the mechanism of V(D)J recombination, we measured the activation of **DNA**-PK by the three **DNA** structures formed during the **cleavage** reaction: open ends, **DNA** nicks, and **hairpin** ends. Although open DNA ends strongly activated DNA-PK, nicked DNA substrates and **hairpin**-ended DNA did not. Therefore, even though efficient processing of **hairpin** coding ends requires DNA-PKCS, this may occur by activation of the kinase bound to the cogenerated open signal end rather than to the **hairpin** end itself.

L24 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999102955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9885569
TITLE: **Hairpin** coding end opening is mediated by RAG1 and RAG2 proteins.
AUTHOR: Besmer E; Mansilla-Soto J; Cassard S; Sawchuk D J; **Brown G**; Sadofsky M; Lewis S M; Nussenzweig M C; Cortes P
CORPORATE SOURCE: Laboratory of Molecular Immunology, Rockefeller University, New York, New York 10021, USA.
SOURCE: Molecular cell, (1998 Dec) 2 (6) 817-28.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990209
Last Updated on STN: 19990209
Entered Medline: 19990126

AB Despite the importance of **hairpin** opening in antigen receptor gene assembly, the molecular machinery that mediates this reaction has not been defined. Here, we show that RAG1 plus RAG2 can open DNA hairpins. **Hairpin** opening by RAGs is not sequence specific, but in Mg²⁺, **hairpin** opening occurs only in the context of a regulated cleavage complex. The chemical mechanism of **hairpin** opening by RAGs resembles RSS cleavage and 3' end processing by HIV integrase and Mu transposase in that these reactions can proceed through alcoholysis. Mutations in either RAG1 or RAG2 that interfere with RSS **cleavage** also interfere with **hairpin** opening, suggesting that RAGs have a single active site that catalyzes several distinct **DNA cleavage** reactions.

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